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A NEW URINE TEST

Z. Klin. Med. (Journal of Clinical Medicine)
No. 5, 1882-1883,
Pages 285-288

Prof. Dr. P. Ehrlich

The diazo compounds, which result from the amido compounds of the aromatic series through the action of nitrous acid, as we know, are capable of readily combining into dyestuffs with a large number of bodies, particularly the mono-, di-, and polyphenols, as well as the primary, secondary, and tertiary mono- and diamines of the aromatic series.

This reaction, which is being applied most widely in this technique recently and which we owe to a wealth of yellow, orange-red, and brown dyestuffs, also seemed to be suitable for medical use. It was to be expected that the secretions and excretions of the human body, primarily however urine, might contain substances which would produce color reactions with the diazo compounds. More specifically, according to Witt's Law, we could expect here that the color reaction occurs in an alkaline solution when the conjugated substance suspended in the urine is an acid and that it occurs in an acid solution when it is a base. For instance, if we add a basic body, for instance anilin, to a solution of diazobenzol, then the yellow coloration of the developing amidobenzol occurs already in the acid solution while the oxyazobenzol, resulting from the combination of phenol and diazobenzol, reveals its color characteristics only when the solution is alkalized.

Indeed, my expectations were confirmed and I found color reactions in the urine which seemed suitable for clinical and diagnostic purposes because of their significance. According to the method of Viktor Meyer, I did not start with the crystallized diazo bodies, which are difficult to obtain; instead, I directly used solutions in which diazo bodies had developed under the influence of nitrites and mineral acids. As initial material I used sulfanilic acid (para amidobenzolsulfo acid (the latter was procured from C.A.F. Kahlbaum)) on the basis of the investigations of Peter Griess: I did this because this sulfanilic acid is smoothly converted into the corresponding diazo compound even without consideration of the special precautionary rules, cooling, and so on, and because it is distinguished rather favorably in this respect from the other compounds, anilin, toluidine, etc.

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I made the solution in such a way that I heavily acidified a larger volume of water, about 500 cc, with pure nitric acid (30-50 cc); I added so much of it as was difficult to dissolve sulfanilic acid that a surplus remained on the bottom. A few granules of sodium nitrite are then dissolved in water in a separate beaker and the solution is gradually mixed in with the former while stirring. The liquid thus obtained--which hereafter I will briefly refer to as the reagent--contains small quantities, almost only traces, of sulfodiazobenzene which produce the reaction that I will describe shortly, as well as the sulfanilic acid, which has no disturbing effects whatever, and nitric acid which has a favorable influence. It does not contain any free nitrous acid. The reagent described will retain its effectiveness for a longer time, especially when the weather is not too hot, and can be used in the summer for 2-3 days and in the winter up to 5 days.

If we fill one third of a test tube with normal urine and if we add the same volume of reagent, we sometimes see no noticeable changes at all and sometimes the entire liquid turns yellowish. If we now add ammonia or potash lye, then we observe a slight change in the color; it turns yellow and sometimes also orange; but the coloration is never strong enough to give the foam, which develops when we shake the liquid, a coloration of its own. If we allow the urine to stand for a longer time, the precipitated rock salts will sometimes form a loose and sometimes a more solid layer on the bottom which does not reveal any definite coloration.

Pathological urines, on the other hand, depending upon the underlying disease, reveal different color reactions and I will only discuss one of these which I think is most interesting here.

If we mix this kind of urine with the reagent in the manner described, then we will sometimes see no change at all and sometimes a very definite yellowish development, as in the case of normal urine. But if we add ammonia, then we get a very intensive carmine-red or scarlet color in certain pronounced cases; the shading of this color can be judged not so much as we look through the test tube than as we observe the foam. If we allow urine of this type to stand for 12 hours, then we can see that the uppermost layers of the precipitate sometimes reveal a wider and sometimes a narrower zone in which we have a very intensive dark coloration. This coloration in some cases is a pure green and in other cases it is greenish-blackish or violet; the latter is sometimes also due to a red precipitate found in normal urine.

I followed this red reaction--which I shall refer to with R for the sake of brevity--in a very large number of diseases and I was able to establish a certain lawfulness and regularity in the occurrence of this reaction. First of all I found that, with the exception of one disease, Phthisis pulmonum, the occurrence of this R is connected with febrile processes. I myself always found negative results in investigating a wide variety of diseases, such as chlorosis, anemia, chronic stomach catarrh, Carcinoma ventriculi, Ileus, Colica saturnina, nephritis, heart defects,

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diseases of the brain and the spinal cord, cirrhosis of the liver, and so on, in short, all of the field of internal pathology, to the extent that it is not connected with any fever.

In contrast to this we have diseases that do involve fever. These we can classify in three groups.

(1) Diseases in which R occurs constantly; (2) diseases in which R occurs more frequently or less rarely, depending upon the type of disease; (3) diseases in which it occurs almost never.

The first group includes the exanthematous processes, which only Typhus abdominalis was investigated in sufficient numbers of cases exceeding well over 60, as well as measles.

The third group includes pneumonia and diphtheria.

The second group includes erysipelas, military tuberculosis, septico-pyemia, pleuritis, scarlet fever, Intermittens, and others.

Statistics prepared in connection with a lecture delivered quite some time ago to the Charite Society, involved only a part of my investigation material and produced the following results.

Among 22 cases of Typhus abdominalis, R was missing only in one case; 5 measles cases revealed R 5 times; 35 cases of Phthisis pulmonum 28 times; of 7 cases of Erysipelas cap, it was found 4 times; among 12 cases of Pleuritis exsudativa, it was found 6 times; in 2 cases of Endocarditis ulcerosa it was found once; in 9 cases of diphtheria faucium it was found only once in a rather slightly indicated fashion; and in 20 cases of croupous pneumonia, it was found only 3 times. Of these three cases, one case was complicated with a Erysipelas, another one was caused by a trauma and was connected with lung gangrene and this left only one typical case out of 20 that revealed R.

My later experiences, which have not yet been arranged statistically, are quite in keeping with these figures. In particular, I never missed the reaction in measles and, as far as I recall, I missed it only in two or three cases in my very voluminous typhus material. One of these cases, which is currently recovering, involved a very light case of Typhus abdominalis in which the fever never exceeded a temperature of 39° and in which the general physical condition therefore was only slightly altered. In this same case I furthermore had a pronounced polyuria (2,000-3,000 cc) with a very low uric acid weight (1005) and this circumstance might possibly have caused the latency of R because of the heavy dilution.

Of course, it is very important to determine during which period of each disease the R occurs because the clinical evaluation of this R can be accomplished only if we consider the time factor.

Let us begin first of all with Typhus abdominalis.

In many cases of this disease we can observe R throughout the entire duration of the sickness, indeed, it may last 1-2 days beyond the definite fever drop in such cases. In other, likewise by no means rarer cases, the R extends over the entire first stage of the disease, such as it is described by high temperature and by the only slightly remitting character of the fever, in order then to disappear with the beginning of the stage of remission. Less frequently we find that R does not last through the entire period of the first stage; in some cases we no longer observe it 3-4 or even perhaps 5 days before the start of remission. Cases in which the time duration of R is even more limited are very rare; here the R can be observed only during the first 3-4 days and, in my experience, these were light cases as a rule. I was unable to determine in my material whether R occurs already during the first two days of sickness but I certainly observed it on the 3rd and 4th days.

In the case of measles, R may be missing during the stage of eruption and full development; but it is found constantly only during the first days of the desquamation stage. Accordingly, it seems as if the substance that produces the reaction is formed during the fever period in the body but that it is retained there and that it was separated only after the crisis had taken place, as it happens in the case of cooking salt.

In pulmonary tuberculosis, which reveals so many different clinical pictures, I want to describe only two borderline cases--first of all, the acute fusion of the lungs which quickly ends in death and phthisis which extends over several years. In the case of the former, the R usually is found in the most pronounced fashion during the entire course of the diseases; in the latter, we have intervals without any reaction, for many months and perhaps even years, alternating with sometimes longer and sometimes shorter periods of times during which R does turn up. When the patients finally die due to the advance of the lung disease and not due to any other complications, then R usually has existed for a longer time before death. Clinical observation teaches us that the periods, during which the R occurs, coincide with exacerbations of the process which, even if the physical examination does not reveal any positive findings, nevertheless are usually clearly marked by fever movement, loss of strength, and nighttime perspiration.

We might emphasize here that, in contrast to all of the other diseases, the R need not necessarily be connected with fever in the case of Phthisis pulmonum; we are therefore justified--in any and every case which presents a pronounced reaction for a longer time without any fever phenomena--to assume with great probability that we are dealing with phthisis.

I believe I may draw the following conclusions from the data here:

1. The reaction is one of the most constant characteristics of Typhus abdominalis from the middle of the first week onward, so that an absence of this reaction would seem to cast doubt upon a diagnosis of this disease.

3. Cases of Typhus abdominalis, in which the reaction is only little pronounced and confined to a short time, as a rule are very light cases.

4. If the reaction stops during the first stage of typhus, with any complications with diseases of the second group (pneumonia), then we can expect the development of remitting temperatures during the next 3-5 days.

5. Of course, the reaction cannot be used for the differential diagnosis between Typhus abdominalis and the diseases of the second group.

6. The occurrence of the reaction in Pneumonia crouposa points to the existence of complications.

7. In Phthisis pulmonum, the occurrence of the reaction is a signum malignum [a serious sign].

8. Long-lasting reactions without fever point to pulmonary tuberculosis.

A detailed description, accompanied by the pertinent disease observations and curves, will be published in the coming Charite-Annalen [Charite Yearbook].